



Original Research Article

A Cross-sectional study on comorbid depression among epileptic adults: experience from a tertiary hospital in Southern India

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ABSTRACT

Background: Epileptic patients suffer from multiple comorbidities resulting in a poor quality of life. Depression is one of the most important and often under-recognized comorbidity among epileptic patients. We aimed to study the prevalence of depression among epileptic adults and also tried to identify potential risk factors predisposing to depression in epilepsy.

Materials and Methods: This was a cross-sectional study on the consecutive epilepsy patients (>18 years) attending our Neurology department between January-2018 to December-2018. All the demographic and clinical details were recorded in the predefined study proforma. Patient Health Questionnaire-9(PHQ-9) was used to screen for depression among epileptic patients. Statistical analysis was done using SPSS software and risk factors associated with depression were considered significant if the p-value ≤ 0.05 .

Results: A total of 300 epileptic adults were enrolled in this study. The mean age of the study subjects was 38-years (range:18-85 years) with a male predominance (M:F-1.7:1). Majority in the epileptic cohort (62%) had secondary education and 14% had primary education. Only 3%(8/300) were postgraduates. Almost half of these epileptic patients were unmarried and one third remained unemployed. Eighty-five percent of the study patients had generalized epilepsy while the rest 15% had focal epilepsy. The mean PHQ score was 8.76 (SD-5.99; Range:0-24) with more than two-thirds of the patient (69%) screened positive for depression. Age>50-years (p-0.004), frequent breakthrough seizures(p-0.000), patients on polytherapy(p-0.000), and poor compliance to anticonvulsants (p-0.000) were found to be significant risk factors for depression in epileptic patients.

Conclusion: Depression is common in epilepsy and awareness among clinicians about this comorbidity is important. Active screening for depression in epilepsy can lead to early interventions resulting in a better quality of life.

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1. Introduction

Epilepsy is a common chronic and disabling neurological condition with India being home to one-eighth of epilepsy patients worldwide.¹ Depression is one of the leading cause of disability adjusted life years (DALY) across the globe as per World Health Organisation (WHO).² Epidemiological studies confirm that depression in epilepsy is associated with poor treatment adherence, poor quality of life, unemployment, lower educational status, and increased

burden on health care services.^{3,4} Also, the frequency of depression is significantly high among epileptic adults compared to patients with chronic ailments like diabetes, bronchial asthma, and multiple sclerosis. These variations in the prevalence of depression among different illnesses can be partially explained by the different study settings including criteria and instruments used to diagnose depression.⁵ The pathogenic link between depression and epilepsy is also poorly understood. Cultural factors, including familial support and coping styles, have been suggested to play a role in determining the risk of depression in patients living with epilepsy (PWE).⁶ Knowledge about

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depression in epilepsy from different cultural settings might potentially impact the clinical evaluation, management, and may help in the understanding of the factors leading to depression in epilepsy or vice versa, paving the way for newer treatment targets in both conditions. We present here details of our study which looked at the prevalence of depression and risk factors predisposing to depression among epileptic adults at a tertiary hospital in Southern India using a validated screening tool.

2. Materials and Methods

This was a cross-sectional study conducted at the Department of Neurology, Govt. T.D. Medical College, Alappuzha between January-2018 to December 2018 on adults (>18 years) with electroencephalographically confirmed epilepsy requiring treatment with one or more antiepileptic drugs. The sample size is calculated using the formula $4PQ/d^2$ where $P=25$,⁷ $Q=100-P$, and d is 5 (20% of P). Accordingly a representative sample was found to be 300. Epileptic patients with a family history of psychiatric illness, delirium, any other systemic illness like diabetes, heart, lung, liver, or renal disease, substance abuse including alcohol use disorder were excluded from the study. All patients / their relatives were interviewed followed by a complete clinical examination of the patients. Clinical and demographic information including treatment details of the epileptic study cohorts were recorded in a predefined study proforma. Patient Health Questionnaire-9 was used to screen depression in our epileptic study cohorts. The presence and the severity of depression in patients and controls were evaluated using the Patient Health Questionnaire 9 (PHQ-9). The PHQ-9, is comprised of 9 items, is self-administered, and is an acceptable method for depression severity assessment. The PHQ-9 has the potential of being a dual-purpose instrument that, with the same 9 items, can establish depressive disorder diagnoses as well as grade depressive symptom severity. It is also valid for the screening of depression in adults with epilepsy. The PHQ-9 rates the frequency of symptoms of depression over the past 2 weeks on a 0–3 scale. The final score is calculated from the sum of each answer, with a minimum score of 0 points and a maximum of 27 points. The final scores computed were used to grade these epileptic patients into having no depression (score:0-4), mild depression (score:5-9), moderate depression (score:10-14), moderately severe (score:15-19), and severe depression (score:20-27) as per the prepared proforma and then.

2.1. Statistical analysis

The data collected were analyzed using SPSS software version 23. Descriptive statistics (frequencies, tables, percentages, and means) were computed to explain the socio-demographic characteristics, clinical variables,

and depression in patients with epilepsy (PWE). The quantitative variables were expressed in mean with standard deviation and median with an interquartile range as appropriate. Qualitative variables were expressed as proportions or percentages. Fischer exact test, Chi-square test, and Mann Whitney U tests were used as appropriate to find out the association of factors predicting depression in epileptic patients. The p-value of ≤ 0.05 was considered as statistically significant. In multivariate analysis, we included variables with a p-value ≤ 0.05 on bivariate analysis. Confidence intervals (CI) for ORs were derived from the regression model.

3. Results

3.1. Demographic profile (Table 1)

A total of 300 epileptic adults were enrolled in our study. The mean age of the study subjects was 38-years (SD-14.81; Range 18-85 years). Majority (63%) were males with only secondary school education (66%). Fourteen percent of the patients had studied upto primary school and only 3% were postgraduates. Close to half of the epileptic study cohorts remained unemployed (45%). Also, there were around one-third of the epileptic patients (30%) who remained unmarried.

3.2. Clinical characteristics of the epileptic cohort (Table 2)

Among this epileptic cohort, 85% had generalized epilepsy and 15% had focal epilepsy. Majority were on monotherapy (69%) for seizure control. Poor drug compliance was noticed among one-fourth of the study patients. Breakthrough seizures in the preceding year were noticed in 78% of the epileptic cohort, while the rest 22% remained seizure-free. More than one-fourth (27%) of the patients had a normal interictal EEG, 19% had a generalized spike and slow-wave discharges and 5% had a focal spike and slow-wave discharges in EEG. Of the study population, 73% had good drug compliance while 27% had poor drug compliance.

3.3. Prevalence of depression in epilepsy

Depression was assessed using PHQ 9 score in the study. The mean PHQ score was 8.76 with a standard deviation of 5.99 (range-0-24). Among 300 patients with epilepsy 206(69%) had depression. Mild depression was noticed in 26% of the patients, 23% had moderate depression, 13% had moderately severe depression, 7% had severe depression (Table 2).

3.4. Factors associated with depression in epilepsy (Table 3)

On bivariate analysis, advanced age (>50 years) (p=0.004), breakthrough seizures (p=0.000), polytherapy (p=0.000), and poor drug compliance (p=0.000) were found to be significantly associated with depression in epileptic adults. Gender, educational status, marital status, type of seizure among epileptic cohorts had no bearing on depression. On multivariate analysis advanced age(>50 Yrs) and polytherapy was found to have an association with depression.(Table 4)

Table 1: Demographic profile of the epileptic study cohort

Demographic factors	Frequency n-300	Percentage (%)
Age		
18-20 yrs	38	13
21-30 yrs	78	26
31-40 yrs	72	24
41-50 yrs	52	17
51-60 yrs	32	11
>60 yrs	28	9
Gender		
Male	118	62
Female	112	38
Education		
Primary	42	14
Secondary	198	66
Graduate	52	17
Post Graduate	8	3
Occupation		
Employed	116	55
Unemployed	134	45
Marital status		
Married	210	70
Unmarried	90	30

4. Discussion

We aimed to study the prevalence of depression among epileptic adults and to analyze the risk factors predisposing to depression in epilepsy. Majority of the enrolled epileptic patients were in their 3rd decade of life (mean age-38years) with a male predominance (male: female ratio-1.68) similar to studies from various parts of India.^{8,9} In an LMIC like India, male predominance would be expected due to better utilization of health care facilities by males compared to females. Also, females have poor access to health care due to certain sociocultural norms and household responsibilities. A recent study however noticed a higher prevalence of epilepsy among Indian females which may indicate changing social attitudes in certain parts of the country.¹⁰ Western studies also report a similar marginally lower incidence of epilepsy and unprovoked seizures in

Table 2: Clinical characteristics of the epileptic cohort

Clinical variables	Frequency n-300	Percentage (%)
Seizure frequency		
No breakthrough seizure	66	22
Breakthrough seizure	234	78
Type of seizure		
Generalized Epilepsy	254	85
Focal Epilepsy	46	15
Antiepileptics		
Monotherapy	206	69
Polytherapy	94	31
Compliance to antiepileptics		
Good compliance	220	73
Poor compliance	80	27
Depression in Epilepsy		
Patients with out Depression	94	31
Patients with depression	206	69
PHQ Score grading of depression in epilepsy		
No depression (0-4)	94	31
Mild depression (5-9)	78	26
Moderate depression (10-14)	68	23
Moderately severe depression (15-19)	40	13
Severe Depression (20-27)	20	7

females than males.¹¹

There are a lot of stigmas associated with epilepsy and unemployment among epileptics is the main result of such social stigma. The overall unemployment rate among the general population reported across the state of Kerala is only 9.43%.¹² In our study, 45 % of the epileptic adults remained unemployed similar to the high unemployment rate (58%) among epileptics reported by Senthil et al.¹³ Difficulty to engage in jobs which may pose threat to their life in case of a breakthrough seizure may be another reason for unemployment among epileptics. Even when employed epileptic adults suffer discrimination, poor performance, increased stress, frequent absenteeism, and finally loss of job. The situation worsens when a patient with epilepsy had epileptic attacks in the workplace that results in social stigma and pushing one to low-income assignments, sometimes even leading to job termination.¹³

Children with epilepsy, especially in rural settings often do not get into schools, have difficulties in coping, exhibit drowsiness and behavioral problems, experience decreased attention, and have poor academic performance. The state of Kerala boasts the highest overall literacy rates (>90%) compared to majority of the other states in India.¹⁴ Our findings of lesser literacy rates among epileptic adults corroborated well with the findings of Nair et al. who showed only 50% of their study subjects to have attained only secondary school education.⁸ Patients with epilepsy (PWE) face profound social isolation and also they have limited prospects for education, employment,

Table 3: Bivariate analysis of risk factors associated with depression in epilepsy

Risk factors	Depression		p-value
	No	Yes	
Age			
≤50 yrs	84	156	0.004
>50 yrs	10	50	
Gender			
Male	56	132	0.454
Female	38	74	
Education level			
Primary & Secondary	78	162	0.384
Graduate & Postgraduate	16	44	
Occupation			
Employed	50	116	0.614
Unemployed	44	90	
Marital status			
Married	64	146	0.625
Unmarried	30	60	
Seizure frequency			
No breakthrough seizure	38	28	0.000
Breakthrough seizure	56	178	
Type of seizure			
Generalized epilepsy	80	174	0.886
Focal epilepsy	14	32	
EEG			
No epileptiform discharges	68	156	0.531
Epileptiform discharges	26	50	
Epilepsy Treatment			
Monotherapy	86	120	0.000
Polytherapy	8	86	
Antiepileptic Drug compliance			
Good compliance	94	126	0.000
Poor compliance	0	8	

Bold indicates statistically significant p-values

Table 4: Multivariate analysis of risk factors associated with Depression in Epilepsy

Variables	Odds Ratio (OR)	Confidence Interval (CI)	p-value
Age > 50 years	0.354	0.162-0.773	0.009
Poor compliance to antiepileptics	0.000	0.000	0.996
Polytherapy	0.409	0.171-0.977	0.044
Breakthrough seizures	0.000	0.000	0.997

Bold indicates statistically significant p-values

and marriage thus making them physically, emotionally, and economically vulnerable. Also, lower marriage rates, delayed marriage especially among females, suspended marriage, and higher divorce rates were noticed among PWE as compared to the general population.¹⁵ In our study, one-third of patients with epilepsy were unmarried. Higher perceived stigma was attributed to epileptic patients remaining unmarried.¹⁶

Depression is the most common inter-ictal psychiatric disorder with a lifetime prevalence of 40 to 60%.¹⁷ Higher prevalence of depression among PWE was also noticed in our study which corroborated well with major studies from India.^{8,18} Although majority of the western studies report a lower frequency of depression in epilepsy in the range of 5%–36%, developing countries such as Pakistan (60%), Korea (62%), and Nigeria (85%) report a higher prevalence of depression among PWE.^{19,20} Patients with epilepsy are known to have comorbid affective disorders and a higher risk for suicide compared with the general population. Epilepsy, depression, and suicidal behavior have been shown to have common pathogenic mechanisms in their etiology. The association between epilepsy, suicidal behavior, and depression was using the comprehensive database of all suicides (n=1877) committed in northern Finland during the years 1988-2002 with information on all hospital-treated somatic and psychiatric disorders. Hospital-treated epilepsy occurred in 1.3% of the victims. Compared with other suicide victims, those with epilepsy were more often female, were older, and had significantly more often suffered from depression. Epilepsy was first diagnosed 8.8 (3.9-11.6) years before suicide, and depression, about 1 year after epilepsy diagnosis. Interictal depression among patients with chronic epilepsy is often classified as atypical or chronic depression, or it can mimic a dysthymic disorder. Therefore, diagnosis and treatment of depression among patients with epilepsy constitute a great challenge in clinical practice.²¹ A possible explanations for the variation in the prevalence of depression in different studies may be due to the use of different tools, (e.g. Hamilton Rating Scale for Depression, Composite International Diagnostic Interview Short Form) use of different cut off points, geographical areas, and cultures of the study subjects. Such a high coexistence of depression among PWE, if unrecognized, can have a negative impact on core outcomes such as inadequate seizure control, quality of life, and increased rates of suicide.

In our study, older epileptic patients (age>50years) had a significantly higher prevalence of depression (p=0.004). Tilahun et al. also noticed a similar association of advanced age with depression in epileptic patients.²² Contrary to this, Joshi et al. found no association of advanced age with depression in epilepsy.²³ Depression among older epileptic patients may be due to their inability to perform the responsibility towards the family, other comorbidities, and a

decline in the neurotransmitters in the aging brain. Female epileptic patients have a higher prevalence of depression compared to males however we didn't find a gender association of depression among our epileptic patients (p=0.454).^{22,24} Lower educational status predisposes to depression in PWE due to poor coping strategies, which in turn leads to social isolation, poor adherence to antiepileptics, school dropout which impairs their cognition and contributes to poorer psychological adjustment in life.^{16,22,25} Also, a higher prevalence of depression was noticed among PWE with unemployment, patients on jobs with lower income, and divorcees.²² However we didn't notice a significant difference in depression among different educational (p=0.384), employment (p=0.614), and marital status (p=0.625) in our study cohorts, which can be partially explained by similar social isolation experienced by these epileptic cohorts irrespective of their demographic status.

Patients with breakthrough seizures had a significantly higher prevalence of depression in our study compared to patients remaining seizure-free (p=0.000) similar to other studies.^{26,27} Also, we noticed epileptic patients on monotherapy were significantly less depressed compared to patients on polytherapy (p=0.000). However, the type of epilepsy did not correlate with depression in our study (p=0.886). Socially unacceptable signs such as urinary and bowel incontinence, foaming from the mouth, and tongue biting may lead the epileptic patient to develop different psycho-social problems including depression.¹⁶ Thus, good seizure control in epilepsy patients may give a positive psychological impact and further help in improving their self-esteem. Suljic et al. also noticed moderate to severe depression in only one-third of their epileptic patients treated with monotherapy whereas 60% of PWE on polytherapy had depression.¹⁷ PWE on polytherapy usually suffers from uncontrolled seizures, which itself predisposes them to more depression in addition to antiepileptic side effects. Sometimes, pseudo-seizures associated with true seizures may be wrongly interpreted as refractory epilepsy by the clinician leading to polytherapy, in turn, resulting in depression among epileptic patients.²⁸

Epileptic patients with good adherence to prescribed antiepileptics had significantly lesser depression (p=0.000) similar to other studies.²⁴ A bidirectional interaction exists between epilepsy and depression with ~60% of PWE developing depression and depression also increasing the risk of epilepsy up to 3–7 fold. Also, depression in PWE itself can lead to poor adherence to drugs due to the “hopelessness” component.

5. Limitations of the study

The cross-sectional nature of our study design may not confirm a definitive cause and effect relationship. Another limitation of the study includes sample study population were recruited from a tertiary care referral center which

might not be a true representation of the depression among PWE in the community. PHQ-9 questionnaire used in this study is a very basic tool to assess depression which might have overestimated the prevalence of depression in PWE. The use of varied treatment regimens in clinical practice might have complicated this analysis.

6. Conclusions

Depression is a common comorbid condition in epilepsy which may be linked to various factors like advanced age (>50 yrs), increased seizure frequency, drug compliance, and polytherapy. Timely recognition and early intervention are the essence to avert multiple complications, including the possibility of worsening the seizure disorder, increased suicidal risk, poor quality of life, poor tolerance to AEDs, and increased economic burden to the family and society. Awareness among clinicians about the high prevalence of depression among epilepsy patients is a must. Screening patients with epilepsy can lead to early detection and treatment of depression.

7. Source of Funding

None.

8. Conflict of Interest

None.

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